

WE CLAIM:

1. The compound 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid monosodium salt having water content of 1.3 % to 11.7%.
2. A hydrate form of a compound of claim 1 which is any of the hydrate forms selected from the group that consists of 1/4 hydrate, 1/3 hydrate, hemihydrate, 2/3 hydrate, 3/4 hydrate, monohydrate, 5/4 hydrate, 4/3 hydrate, 3/2 hydrate, and dehydrate.
3. The compound 4-amino-1-hydroxybutylidene-1, 1-bisphosphonic acid monosodium salt having water content of 5.1 % to 7.0%.
4. The compound according to claim 3 having water content of about 6.2%.
5. Alendronate monosodium monohydrate.
6. The compound according to claim 3, which is characterized by peaks in the powder xray diffraction at values of two theta of 12.7 ± 0.2 , 16.2 ± 0.2 , 17.3 ± 0.2 , 17.6 ± 0.2 , 24.8 ± 0.2 , and 25.5 ± 0.2 .
7. A method of preparing the compound of any of claims 3 through 6 comprising the steps of:
 - a) reacting one equivalent of 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid with one equivalent of sodium base in a lower alkanol comprising 5 to 200 equivalents of water; and
 - b) isolating said compound of any of claims 3 through 6.
8. A method according to claim 7 wherein the compound 4-amino-1-hydroxybutylidene- 1, 1-bisphosphonic acid is in a monohydrate form.
9. A method according to claim 7 wherein the lower alkanol is selected from the group consisting of methanol, ethanol and isopropanol.
10. A method according to claim 7 wherein the sodium base is selected from the group consisting of sodium hydroxide, sodium methoxide and sodium ethoxide.
11. A method according to claim 7 wherein the compound 4-amino-1-hydroxybutylidene-

- 1, 1-bisphosphonic acid is in an anhydrous form.
12. A method of preparing the compound of any of claims 3 through 6 comprising the steps of:
- a) treating 4-amino-1-hydroxybutylidene-1, 1-bisphosphonic monosodium salt in a lower alkanol with 20-40 equivalents of water; and
 - b) isolating said compound of any of claims 3 through 6.
13. A method according to claim 12 wherein the lower alkanol of step a) is ethanol.
14. A method of preparing the compound of any of claims 3 through 6 comprising the steps of:
- a) treating 4-amino-1-hydroxybutylidene-1, 1-bisphosphonic disodium salt in a lower alkanol with 20-40 equivalents of water, and one equivalent of alendronic acid; and
 - b) isolating said compound of any of claims 3 through 6.
15. A method according to claim 14 wherein the lower alkanol of step a) is ethanol.
16. A method of preparing the compound of any of claims 3 through 6 comprising the steps of:
- a) treating 4-amino-1-hydroxybutylidene-1, 1-bisphosphonic trisodium salt in a lower alkanol with 20-40 equivalents of water and two equivalents of alendronic acid; and
 - b) isolating said compound of any of claims 3 through 6.
17. A method according to claim 16 wherein the lower alkanol of step a) is ethanol.
18. A method of preparing the compound of any of claims 3 through 6 comprising the steps of:
- a) treating 4-amino-1-hydroxybutylidene-1, 1-bisphosphonic tetrasodium salt in a lower alkanol with 20-40 equivalents of water and three equivalents of alendronic acid; and

- b) isolating said compound of any of claims 3 through 6.
- 19. A method according to claim 18 wherein the lower alkanol of step a) is ethanol.
- 20. A method according to claim 12 in which the 4-amino-1-hydroxybutylidene-1, 1-bisphosphonic sodium salt is a monosodium salt trihydrate.
- 21. A compound according to claim 3, which is characterized by peaks in the powder x-ray diffraction at values of two theta of 9.3 ± 0.2 , 12.4 ± 0.2 , 13.5 ± 0.2 , 26.3 ± 0.2 and 30.0 ± 0.2 .
- 22. A method of preparing the compound of claim 21 comprising the steps of:
 - a) treating 4-amino-1-hydroxybutylidene-1,1-bisphosphonic monosodium trihydrate with an effective amount of a drying agent; and
 - b) isolating said compound of claim 21.
- 23. A method according to claim 22 wherein the reaction of step a) is performed in ethanol.
- 24. Alendronate monosodium hemihydrate.
- 25. The compound 4-amino-1-hydroxybutylidene-1, 1-bisphosphonic acid monosodium salt having water content of 2.8% to 3.9%.
- 26. The compound according to claim 25 having water content of about 3.2%.
- 27. The compound according to claim 25, which is characterized by peaks in the powder x-ray diffraction at values of two theta of 7.0 ± 0.2 , 9.3 ± 0.2 , and 14.0 ± 0.2 .
- 28. A method of preparing the compound of claim 24 or 25 comprising the steps of:
 - a) treating 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid in a lower alkanol with one equivalent of sodium base and 9 to 15 equivalents of water; and
 - b) isolating said compound of claim 24 or 25.
- 29. A method according to claim 28 wherein the compound 4-amino-1-hydroxybutylidene-1, 1-bisphosphonic acid is in a monohydrate form.
- 30. A method according to claim 28 wherein the lower alkanol is selected from the group consisting of methanol, ethanol and isopropanol.

31. A method according to claim 28 wherein the sodium base is selected from the group consisting of sodium hydroxide, sodium methoxide and sodium ethoxide.
32. A method according to claim 28 wherein the compound 4-amino-1-hydroxybutylidene-1, 1-bisphosphonic acid is in an anhydrous form.
33. The compound 4-amino-1-hydroxybutylidene-1, 1-bisphosphonic acid monosodium salt having water content of 2.5% to 3.5%.
34. The compound according to claim 33, which is characterized by peaks in the powder x-ray diffraction at values of two theta of 9.2 ± 0.2 , 14.2 ± 0.2 , 15.0 ± 0.2 , 17.1 ± 0.2 , 20.7 ± 0.2 , 22.0 ± 0.2 , 22.4 ± 0.2 .
35. A method of preparing the compound of claim 2 or 33 comprising the steps of:
 - a) treating 4-amino-1-hydroxybutylidene-1, 1-bisphosphonic acid in a lower alkanol with one equivalent of sodium base and 17 to 22 equivalents of water; and
 - b) isolating said compound of claim 2 or 33.
36. A method according to claim 35 in which the compound 4-amino-1 - hydroxybutylidene-1, 1-bisphosphonic acid is in a monohydrate form.
37. A method according to claim 35 wherein the lower alkanol is selected from the group consisting of methanol, ethanol and isopropanol.
38. A method according to claim 35 wherein the sodium base is selected from the group consisting of sodium hydroxide, sodium methoxide and sodium ethoxide.
39. The compound 4-amino-1-hydroxybutylidene-1, 1-bisphosphonic acid monosodium salt having water content of 6.4% to 9.0%.
40. The compound according to claim 39, which is characterized by peaks in the powder x-ray diffraction at values of two theta of 12.2 ± 0.2 , 13.3 ± 0.2 , 14.8 ± 0.2 , 15.8 ± 0.2 , 16.3 ± 0.2 , and 17.2 ± 0.2 .
41. A method of preparing the compound of claim 2 or 39 comprising the steps of:

- a) treating 4-amino-1-hydroxybutylidene-1, 1-bisphosphonic acid in a lower alkanol with one equivalent of sodium base and 0 to 4 equivalents of water; and
 - b) isolating said compound of claim 2 or 39.
42. A method according to claim 41 in which the compound 4-amino-1-hydroxybutylidene-1, 1-bisphosphonic acid is in a monohydrate form.
43. A method according to claim 41 wherein the lower alkanol is selected from the group consisting of methanol, ethanol and isopropanol.
44. A method according to claim 41 wherein the sodium base is selected from the group consisting of sodium hydroxide, sodium methoxide and sodium ethoxide.
45. The compound 4-amino-1-hydroxybutylidene-1, 1-bisphosphonic acid monosodium salt having water content of 3.2% to 5.8%.
46. The compound according to claim 45, which is characterized by peaks in the powder x-ray diffraction at values of two theta of 13.1 ± 0.2 , 15.2 ± 0.2 , 16.3 ± 0.2 , 22.3 ± 0.2 , 22.5 ± 0.2 , 23.4 ± 0.2 , and 23.7 ± 0.2 .
47. A method of preparing the compound of 2 or 45 comprising the steps of:
- a) treating 4-amino-1-hydroxybutylidene-1, 1-bisphosphonic acid anhydrous in a lower alkanol with one equivalent of sodium base and 0 to 4 equivalents of water; and
 - b) isolating said compound of claim 2 or 45.
48. A method according to claim 47 in which the compound 4-amino-1-hydroxybutylidene-1, 1-bisphosphonic acid is in an anhydrous form.
49. A method according to claim 48 wherein the lower alkanol is selected from the group consisting of methanol, ethanol and isopropanol.
50. A method according to claim 48 wherein the sodium base is selected from the group consisting of sodium hydroxide, sodium methoxide and sodium ethoxide.
51. The compound 4-amino-1-hydroxybutylidene-1, 1-bisphosphonic acid monosodium salt

- having water content of 1.3 % to 3.1 %.
52. The compound according to claim 51, which is characterized by peaks in the powder x-ray diffraction at values of two theta of 13.0 ± 0.2 , 13.4 ± 0.2 , 14.2 ± 0.2 , 19.1 ± 0.2 , and 19.4 ± 0.2 .
53. A method of preparing the compound of claim 2 or 51 comprising the steps of:
- a) treating 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid in a lower alkanol with one equivalent of sodium base and 3 to 20 equivalents of water; and
 - b) isolating said compound of claim 2 or 51.
54. A method according to claim 53 in which the compound 4-amino-1-hydroxybutylidene-1, 1-bisphosphonic acid is in a monohydrate form.
55. A method according to claim 53 wherein the lower alkanol is selected from the group consisting of methanol, ethanol and isopropanol.
56. A method according to claim 53 wherein the sodium base is selected from the group consisting of sodium hydroxide, sodium methoxide and sodium ethoxide.
57. A method according to claim 53 wherein the compound 4-amino-1-hydroxybutylidene-1, 1-bisphosphonic acid is in an anhydrous form.
58. Alendronate monosodium dihydrate.
59. The compound 4-amino-1-hydroxybutylidene-1, 1-bisphosphonic acid monosodium salt having water content of about 11.7%.
60. The compound according to claim 59, which is characterized by peaks in the powder x-ray diffraction at values of two theta of 9.3 ± 0.2 , 12.4 ± 0.2 , 13.5 ± 0.2 , 26.3 ± 0.2 and 30.0 ± 0.2 .
61. A method for preparing a compound according to claim 58 or 59 comprising the steps of:
- a) treating 4-amino-1-hydroxybutylidene-1, 1-bisphosphonic acid monosodium salt trihydrate with an effective amount of drying agent; and

- b) isolating 4-amino-1-hydroxybutylidene-1, 1-bisphosphonic acid the monosodium salt dihydrate.
62. A pharmaceutical composition comprising a pharmaceutically effective amount of a compound of any of claims 1, 3, 25, 33, 39, 45 and 51.
63. A method for treating and/or preventing bone loss in a subject, comprising the step of administering to said subject in need thereof an effective amount of the pharmaceutical composition as defined in claim 62.
64. A method of preparing the compound of claim 1 comprising the steps of:
- a) reacting one equivalent of 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid with one equivalent of sodium base in an aqueous organic solvent selected from the group consisting of acetone, DMSO, DMF, acetonitrile, alcohols, polyalcohols, polyalcohol ethers, pyridine, sulfolane, N-methyl pyrrolidinone and dioxane, and
 - b) isolating said compound of claim 1.
65. A method of preparing the compound of claim 3 comprising the steps of:
- a) reacting one equivalent of 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid with one equivalent of sodium base in an aqueous organic solvent selected from the group consisting of acetone, DMSO, DMF, acetonitrile, alcohols, polyalcohols, polyalcohol ethers, pyridine, sulfolane, N-methyl pyrrolidinone and dioxane, and
 - b) isolating said compound of claim 3.
66. A method of preparing the compound of claim 25 comprising the steps of:
- a) reacting one equivalent of 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid with one equivalent of sodium base in an aqueous organic solvent selected from the group consisting of acetone, DMSO, DMF, acetonitrile, alcohols, polyalcohols, polyalcohol ethers, pyridine, sulfolane, N-methyl pyrrolidinone

- and dioxane, and
- b) isolating said compound of claim 25.
67. A method of preparing the compound of claim 33 comprising the steps of:
- a) reacting one equivalent of 4-amino-1-hydroxybutylidene-1, 1-bisphosphonic acid with one equivalent of sodium base in an aqueous organic solvent selected from the group consisting of acetone, DMSO, DMF, acetonitrile, alcohols, polyalcohols, polyalcohol ethers, pyridine, sulfolane, N-methyl pyrrolidinone and dioxane, and
- b) isolating said compound of claim 33.
68. A method of preparing the compound of claim 39 comprising the steps of:
- a) reacting one equivalent of 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid with one equivalent of sodium base in an aqueous organic solvent selected from the group consisting of acetone, DMSO, DMF, acetonitrile, alcohols, polyalcohols, polyalcohol ethers, pyridine, sulfolane, N-methyl pyrrolidinone and dioxane, and
- b) isolating said compound of claim 39.
69. A method of preparing the compound of claim 45 comprising the steps of:
- a) reacting one equivalent of 4-amino-1-hydroxybutylidene-1, 1-bisphosphonic acid with one equivalent of sodium base in an aqueous organic solvent selected from the group consisting of acetone, DMSO, DMF, acetonitrile, alcohols, polyalcohols, polyalcohol ethers, pyridine, sulfolane, N-methyl pyrrolidinone and dioxane, and
- b) isolating said compound of claim 45.
70. A method of preparing the compound of claim 51 comprising the steps of:
- a) reacting one equivalent of 4-amino-1-hydroxybutylidene-1, 1-bisphosphonic acid with one equivalent of sodium base in an aqueous organic solvent selected

from the group consisting of acetone, DMSO, DMF, acetonitrile, alcohols, polyalcohols, polyalcohol ethers, pyridine, sulfolane, N-methyl pyrrolidinone and dioxane, and

b) isolating said compound of claim 51.

71. A method of preparing the compound of claim 59 comprising the steps of:

- a) reacting one equivalent of 4-amino-1-hydroxybutylidene-1, 1-bisphosphonic acid with one equivalent of sodium base in an aqueous organic solvent selected from the group consisting of acetone, DMSO, DMF, acetonitrile, alcohols, polyalcohols, polyalcohol ethers, pyridine, sulfolane, N-methyl pyrrolidinone and dioxane, and
- b) isolating said compound of claim 59.